MedicalXpress

Evaluating the accuracy of the Curacao Criteria in diagnosing HHT in children

April 12 2018

Though hereditary hemorrhagic telangiectasia (HHT) is – as the name suggests – a hereditary disorder, most people are not diagnosed with the disease until they are adults because the telltale symptoms often do not develop until patients are in their late teens or early 20s. As a result, there is little data on the efficacy or value of the available diagnostic tools in children and even less on the potential effects HHT may have on them as the disorder progresses.

Researchers led by Raj Kasthuri, MD, associate professor of medicine and director of the UNC HHT Center of Excellence, have begun to fill in some of the details in the story of how HHT affects children. Researchers were particularly interested in the diagnostic power of the Curacao Criteria, a set of clinical characteristics that helps clinicians identify HHT, as it relates to children.

"There haven't been studies looking at the diagnosis of HHT in childhood," said Kasthuri. "Are the criteria that we use for adults also effective for children? Can we use these criteria reliably? Our objective was to get better answers to these questions and then try to develop some recommendations for clinicians who may be considering having a child evaluated for HHT."

HHT is a relatively rare disease, affecting around 1 in 5,000 people, and is characterized by the development of abnormal blood vessels at the level of the capillaries, called telangiectasias. These form on the skin and mucous membranes, and commonly present as red spots on the skin and

nosebleeds that are sometimes very severe.

HHT is diagnosed in one of two ways. The first and most simple is to apply what is called the Curacao Diagnostic Criteria, four criteria that include family history of HHT, severe recurrent nosebleeds, telangiectasias, and involvement of the internal organs with arteriovenous malformations (AVMs). Meeting three or more of these is considered definite HHT. But because several of these develop as a person ages, especially the telangiectasias, the Curacao Criteria can be an imperfect diagnostic tool that requires genetic testing for confirmation.

The multi-center retrospective chart review involved researchers from HHT Centers of Excellence at Yale University, Cincinnati Children's Hospital, St. Louis Children's Hospital and the UNC School of Medicine. The charts of nearly 300 patients ages 0-21 were found to be eligible for the study. The performance of the Curacao Criteria was compared against the gold standard of a HHT-causing mutation identified by genetic testing.

"What we ultimately found after reviewing these charts is that the Curacao Criteria are not accurate in children that meet only one or two of these criteria," said Kristy Pahl, MD, a pediatric hematology oncology fellow at UNC and first author on the study. "We would prefer genetic testing in those children to either confirm or exclude HHT. However, in children that meet 3 or 4 criteria, the criteria are accurate, and genetic testing is not necessary for diagnosis."

Findings also add granularity to the overall picture of the progression and diagnosis of HHT in childhood.

"In the youngest age groups, especially children 0-5 years old, the Curacao Criteria did not correlate with having HHT. As children got older and more symptoms started to develop there was a stronger

correlation between how many criteria they met and a positive genetic test for HHT," said Pahl.

Information like this provides more accurate clinical guidance, which can be especially helpful in places where genetic testing may not be as easily accessible as it is in the US. It also makes it possible to develop better guidelines as to when the clinical diagnosis can be taken as definitive by itself.

"If we can identify a particular age cutoff," said Kasthuri, "and we are able to say that beyond this age you can just resort to clinical diagnosis, the better we get at diagnosing this disease, and the more economically and appropriately we can treat these patients."

This is especially important because the complications from HHT can be very severe, and may include AVMs in the lungs, liver and brain. When someone is diagnosed with HHT these organs must be monitored periodically to screen for AVMs so appropriate treatment can be implemented.

"When someone is diagnosed with HHT, you have to do MRIs of their brain to look for brain involvement. You have to do scans of their lungs to look for lung involvement. There are follow ups to a diagnosis of HHT, which can be very expensive and you don't want to do them unnecessarily," said Kasthuri.

This study also helped to gather information on the progression of organ involvement in children with HHT. The nosebleeds and red spots associated with HHT develop with age but it was not clear if involvement of the internal organs followed a similar timeline.

"What we found is that the timeline of internal organ involvement is not the same timeline as the bleeding manifestations – the nosebleeds – that

happen with age," said Kasthuri. "You can have lung AVMs in childhood that are bad enough that they need to be intervened on. You can have brain involvement in childhood, so screening for internal organ involvement is something that cannot wait until adulthood."

Kasthuri stressed that this is part of why the development of accurate diagnostic guidelines is so important.

"If we can develop good guidelines on how to make the diagnosis of HHT in childhood then we can better manage these patients and also avoid inappropriate imaging studies. There are children who are followed with periodic scans because no one knows if they have HHT or not. But if you can better diagnose definitely one way or the other in childhood then we can prevent unnecessary imaging in those that don't need them and ensure that those who do need screening get it."

Provided by University of North Carolina at Chapel Hill School of Medicine